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Depression in newly diagnosed type 2 diabetes is associated with raised levels of systemic inflammatory markers.

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Background and aims: There is an increased prevalence of depression in type 2 diabetes mellitus (T2DM) which is associated with more frequent diabetes complications and increased mortality. T2DM and macrovascular disease are independently associated with raised levels of circulating inflammatory markers and in non-diabetes participants there is evidence that depression is linked with inflammation. Since inflammation may be the common antecedent of both T2DM and depression and may play a pathogenic role, we tested the hypothesis that patients with new-onset T2DM and depression have higher levels of circulating inflammatory markers than T2DM patients without depression.

Materials and methods: Adults with newly diagnosed T2DM recruited from primary care were assessed for depression using the Patient Health Questionnaire-9 (PHQ-9). Markers of inflammation were measured from fasting blood samples and included: high sensitivity C-reactive protein (hs-CRP), white blood cell count (WBC), interleukin-1 receptor antagonist (IL-1RA). Covariates included socio-demographic factors, adiposity, smoking and HbA_{1c}. Univariate analyses were used to determine relationships between depression and inflammatory markers and multiple linear regressions were used to adjust for covariates.

Results: 1489 data sets were available for analysis; mean [SD] age = 55.4 [11.2] years, 44.9% female, prevalence of depression = 14.7%. Depressed participants were younger at diagnosis (mean [SD] age = 52 [9.9] vs. 56 [11.2] years, $p < 0.001$) but had similar HbA_{1c} (mean [SD] HbA_{1c} = 7.0 [1.5] vs. 7.2 [1.5] %). Inflammatory markers were significantly increased in depressed compared to non-depressed participants; median [IQR] hs-CRP = 3.4 [1.5 - 8.9] vs. 2.6 [1.1 - 6.2] mg/L, $p = 0.002$; median [IQR] WBC = 7.1 [5.7 - 8.6] vs. 6.5 [5.3 - 7.9] $\times 10^9/L$, $p < 0.001$; median [IQR] IL-1RA = 501.6 [334.6 - 786.3] vs. 435.4 [292.0 - 678.2] ng/L, $p = 0.004$. Associations between levels of inflammatory markers and depressive symptoms remained after adjusting for covariates: hs-CRP (standardised $b = 0.10$, $p = 0.002$), WBC (standardised $b = 0.11$, $p < 0.001$), IL-1RA (standardised $b = 0.13$, $p < 0.001$). After one year inflammatory markers remained significantly increased in participants who were depressed at baseline compared with participants who were not depressed at baseline: median [IQR] hs-CRP = 3.5 [1.3 - 7.9] vs. 2.2 [0.9 - 5.0] mg/L, $p < 0.001$. This association also remained after adjusting for covariates: hs-CRP (standardised $b = 0.11$, $p < 0.001$). In those who were depressed at baseline after twelve months there was no difference in levels of inflammatory markers between those with improved depressive symptoms and those without.

Conclusion: Circulating markers of inflammation are significantly elevated in T2DM participants with depression compared to non-depressed T2DM participants, these levels are still raised 12 months later. These consistently increased levels of inflammation and activated innate immunity observed in T2DM with depression may help to explain the persistent increased risk of complications and mortality in this group.